

REMARKS/ARGUMENTS

Claims 1-14 are pending in the above-captioned application.

The following remarks are believed to be fully responsive to the Office Action.

THE REJECTION UNDER 35 U.S.C. 103(a) SHOULD BE WITHDRAWN

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crane, US Patent No. 5,961,952 ("Crane") in view of JP '192 or Schott Gaswerke, DE 29609958 ("DE '958) or Walther, US Patent No. 6,200,658 ("Walther"). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

The Examiner's logic is that Crane teaches "the use of metal complexes as radiopharmaceuticals which are in kit form", and that the person skilled in the art would look to apply "any possible benefits in the same field of endeavour or reasonable pertinent to the problem being solved".

The Examiner also alleges that:

"Clearly, the use of silicon [*Emphasis added*] coated vials is a known advantage in the field of pharmaceuticals and radiopharmaceuticals, and therefore one skilled in the art would obtain these benefits for various pharmaceuticals and/or radiopharmaceuticals, such as, those disclosed by Crane. Therefore the motivation to combine arises from the benefits of the prior art".

Applicants respectfully point out that the Examiner refers to 'silicon' coatings at least 8 times in the Office Action. Silicon is the chemical element Si, whereas the present claims refer to silica which is silicon dioxide or SiO₂. Clearly combinations which teach towards silicon coatings teach away from the present invention. When the Examiner refers to 'silicon coatings', it is not clear whether this is shorthand for 'silicon-containing' or a typographical

error for 'silica'. Please clarify. The latter will be assumed and the response written with that assumption.

Applicants contend that the Examiner's logic is invalid. A prima facie obviousness requires that motivation for the skilled artisan to modify or combine specific references exists. The Examiner's own statements [quoted above] refer to "various pharmaceuticals and/or radiopharmaceuticals" and "such as, those disclosed by Crane" and "reasonably pertinent to the problem being solved".

These points fail to address the key criterion of why the person skilled in the art would specifically choose Crane to combine with, and hence where the motivation exists to apply the silica-coated vials to radiopharmaceutical metal complexes. It is not clear what exactly the specific "benefits" that would be expected for radiopharmaceutical metal complexes are. The Examiner's own statements seem to suggest that the person skilled in the art *could* apply the silica-coated vials to *any* radiopharmaceutical, of which Crane is merely illustrative. This is a weak combination, inadequate for an obviousness attack, since it is based almost exclusively on the vial prior art, with merely passing reference to Crane. Indeed, if the Examiner's logic was followed, then all radiopharmaceuticals would be provided in silica-coated vials, once the prior art in question had published, and no one would contemplate using uncoated vials, since it would be madness to ignore the purported "benefits". In reality, uncoated vials are still very much the norm for radiopharmaceuticals and coated vials (in any form), the exception. This is because coated vials are significantly more expensive, and no one would accept the additional costs for unspecified "benefits" that were not necessary for the specific product. The Examiner's logic is therefore unrealistic.

Applicants also submit that Examiner's argumentation is circular, wherein the purported motivation originates from "benefits" within the vial prior art in isolation, not from the combination [vial prior art] + [Crane]. Applicants contend that no motivation to combine exists because Crane itself does not teach or suggest that the radiopharmaceutical metal complexes described therein suffer from any leaching problems, hence no expectation of success exists. Hence, the (unspecified) 'problem being solved' suggested by the Examiner

does not exist within Crane itself. Furthermore 'reasonably pertinent to the problem' is vague and not the standard applied by the USPTO for an obviousness attack – motivation based on a clear expectation of improved results for the specific combination must be demonstrated.

Applicants also stress that the present invention describes at length how radiopharmaceutical metal complexes suffer from unforeseen or variable problems which are solved using silica-coated vials. See page 4 line 17 to page 9 line 23 of the present specification. These problems were not recognised in the prior art, and hence there was simply no motivation to apply silica-coated vials to radiopharmaceutical metal complexes. The solution to the problem provided by the present claims is believed non-obvious for this reason.

Furthermore, the invention of Crane has many features:

- tert*-butyl Isonitrile ligand
- ^{99m}Tc or $^{186}\text{Re}/^{188}\text{Re}$ metal complex thereof
- solubilization aid
- reducing agent
- pharmaceutically-acceptable carrier
- a non-radioactive italties-butyl isonitrile metal complex precursor
- pharmaceutically-acceptable filler
- vial
- lyophilization aids
- buffers
- stabilization aids
- bacteriostats
- transfer ligand,
- etc.

which are described at Columns 7 and 8 of Crane. The Examiner's obviousness logic would mean that the person skilled in the art would be motivated to improve all aspects of Crane

wherever a claimed "benefit" in a later document was disclosed. On that basis, most if not all the above aspects of Crane would be improved, not just one. Applicants contend that the Examiner has failed to show why the person skilled in the art would select only the vial from this long list of features to seek to improve, and as a consequence choose not to improve all the other aspects even those which Crane teaches as important. Furthermore, it is inconceivable that a person skilled in the art would choose specifically silica-coated vials, when a great variety of alternative coatings (e.g. including silicon-containing polymers such as silicones or silanes) were available, in regular use, each also having "benefits".

The Examiner argues that the person skilled in the art would be motivated to combine Crane and JP'192 to solve absorption problems. Crane, however, specifically teaches "solubilization aids" as an essential feature to solve this problem described therein:

Column 2 lines 33-47 and 56-57,

Column 3 lines 23-33 and 46-47

Column 7 lines 1-26,

The logic of the Examiner's combination is that the 'solubilization aid' taught by Crane would no longer be necessary, since the coated vial would solve the absorption problem. This contradicts the teaching of Crane, would remove an essential teaching of Crane is thus an invalid combination. Applicants therefore contend that the obviousness rejection based on this combination should also be withdrawn.

Thus, Applicants respectfully request that the rejections be withdrawn.

CONCLUSIONS

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

Respectfully submitted,



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